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=> d his

     (FILE 'HOME' ENTERED AT 11:42:34 ON 23 JUN 2000)

     FILE 'HCAPLUS' ENTERED AT 11:42:41 ON 23 JUN 2000
L1           250 S STELLA V?/AU
L2            31 S ZYGMUNT J?/AU
L3             1 S GEORG I?/AU
L4             8 S SAFADI M?/AU
L5             1 S L1 AND L2 AND L3 AND L4
L6             1 S L1 AND L2 AND L4
                 SELECT RN L5 1

     FILE 'REGISTRY' ENTERED AT 11:43:17 ON 23 JUN 2000
L7            50 S E1-50

     FILE 'HCAPLUS' ENTERED AT 11:43:26 ON 23 JUN 2000
L8             1 S L6 AND L7
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Inventor Search

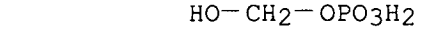
=> d bib abs hitstr

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:117059 HCAPLUS
DN 132:171119
TI Water-soluble prodrugs of hindered alcohols or phenols
IN **Stella, Valentino J.**; **Zygmunt, Jan J.**; Georg, Ingrid Gunda; **Safadi, Muhammed S.**
PA University of Kansas, USA
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000008033	A1	20000217	WO 1999-US17779	19990806

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

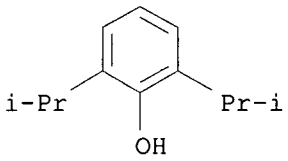
PRAI US 1998-131385 19980807
OS MARPAT 132:171119
AB Water-sol. phosphonooxymethyl esters of drugs contg. aliph. or arom. hindered OH groups are prepd. as prodrugs to improve the bioavailability of the drugs without use of surfactants which lead to severe side effects.
Among the drugs thus rendered water sol. are camptothecin, propofol, cyclosporin A, etoposide, and .alpha.-tocopherol. Thus, propofol was converted via its O-(methylthio)methyl, O-chloromethyl, and O-phosphonooxymethyl dibenzyl ester derivs. to O-phosphonooxymethylpropofol. This compd. had a water soly. of .apprx.500 mg/mL, was nontoxic in rats, was converted to propofol by alk. phosphatase in vitro, and produced anesthesia in dogs in a similar manner to a com. propofol formulation (Diprivan).
IT **16432-39-6DP**, ethers
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(water-sol. prodrugs of hindered alcs. or phenols)
RN 16432-39-6 HCAPLUS
CN Methanediol, mono(dihydrogen phosphate) (8CI, 9CI) (CA INDEX NAME)



IT **1406-18-4**, Vitamin E **2078-54-8**, Propofol

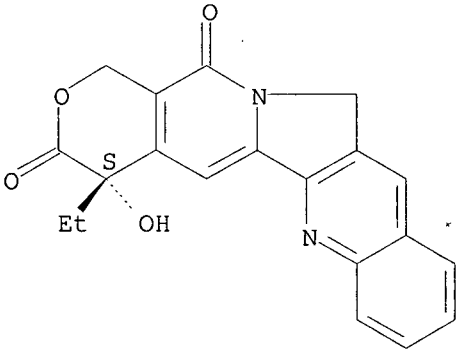
7689-03-4, Camptothecin **7689-03-4D**, Camptothecin, analogs **33419-42-0**, Etoposide **59865-13-3**, Cyclosporin A
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(water-sol. prodrugs of hindered alcs. or phenols)
RN 1406-18-4 HCAPLUS
CN Vitamin E (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 2078-54-8 HCAPLUS
CN Phenol, 2,6-bis(1-methylethyl)- (9CI) (CA INDEX NAME)



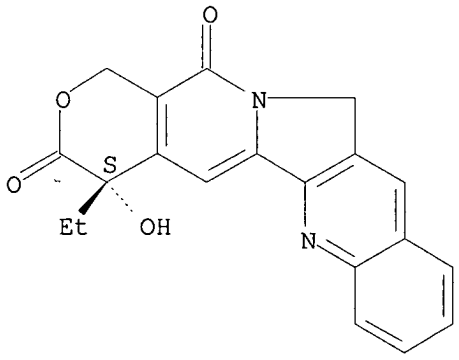
RN 7689-03-4 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-hydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



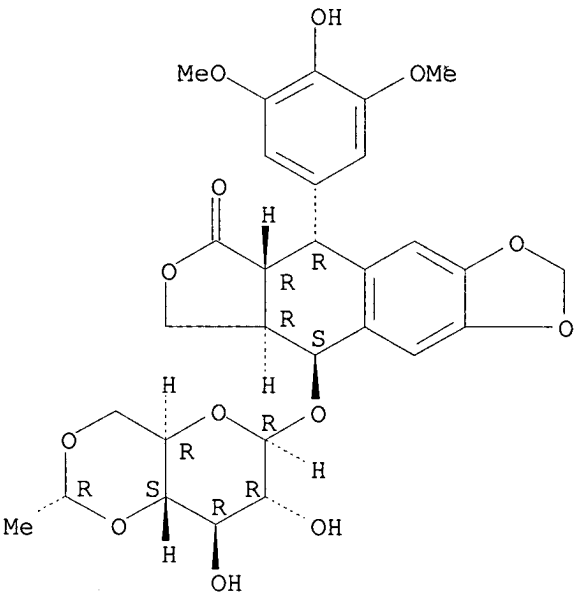
RN 7689-03-4 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-hydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 33419-42-0 HCAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



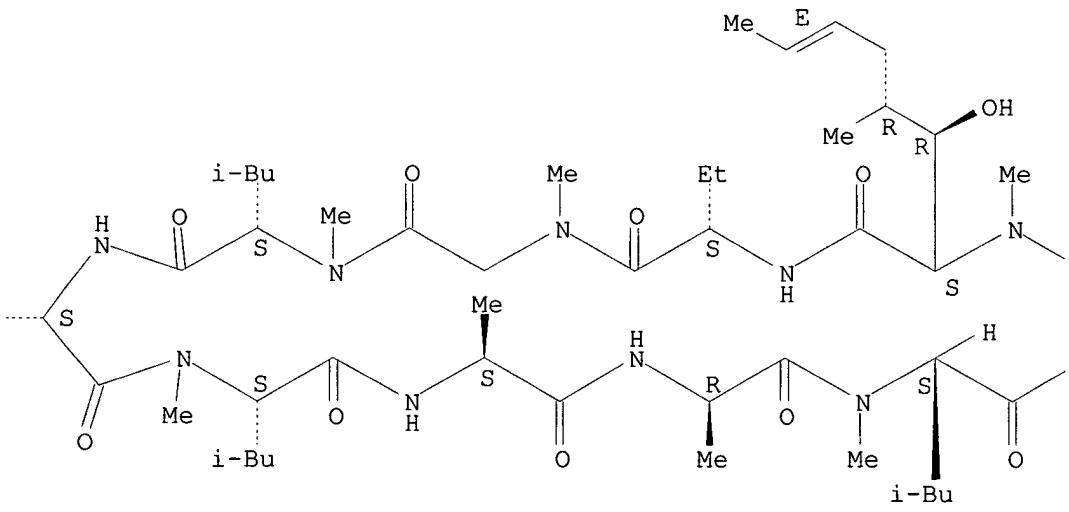
RN 59865-13-3 HCAPLUS
CN Cyclosporin A (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

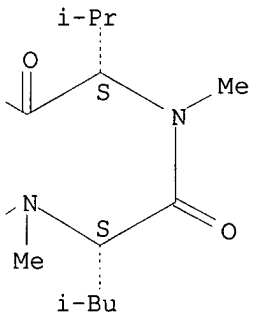
PAGE 1-A

i-Pr

PAGE 1-B



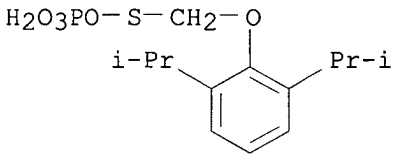
PAGE 1-C



IT **258516-87-9P 258516-89-1P 258516-91-5P**
258516-93-7P 258516-95-9P 258516-97-1P
258516-99-3P 258517-01-0P 258517-02-1P
258517-03-2P 258517-04-3P 258517-05-4P
258517-08-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(water-sol. prodrugs of hindered alcs. or phenols)

RN 258516-87-9 HCAPLUS

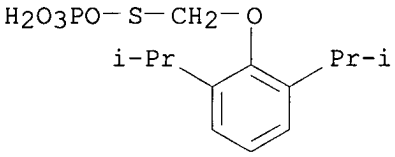
CN Phosphoro(thioperoxoic) acid, OS-[[2,6-bis(1-methylethyl)phenoxy]methyl] ester, disodium salt (9CI) (CA INDEX NAME)



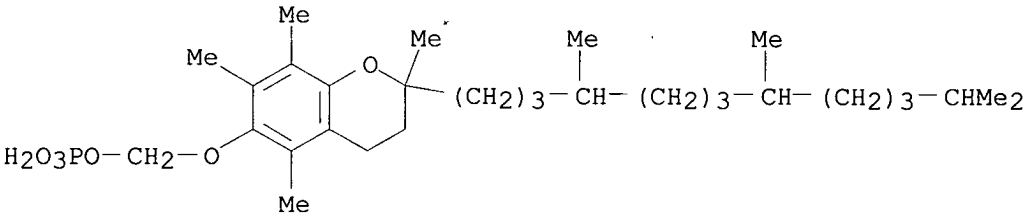
● 2 Na

RN 258516-89-1 HCAPLUS

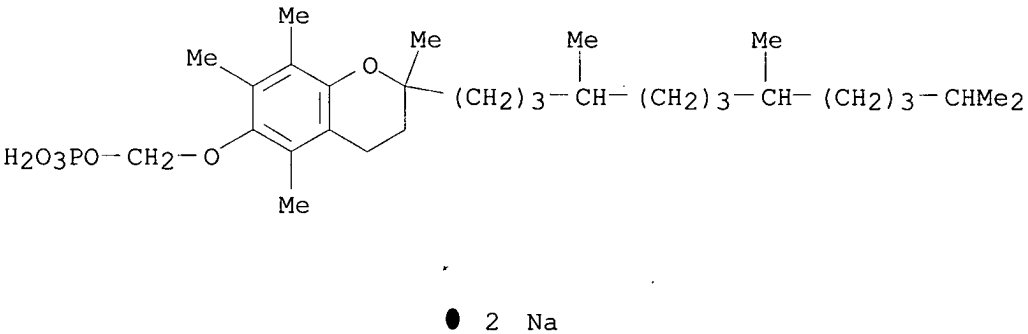
CN Phosphoro(thioperoxoic) acid, OS-[[2,6-bis(1-methylethyl)phenoxy]methyl] ester (9CI) (CA INDEX NAME)



RN 258516-91-5 HCAPLUS
CN Methanol, [[3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl]oxy]-, dihydrogen phosphate (9CI) (CA INDEX NAME)

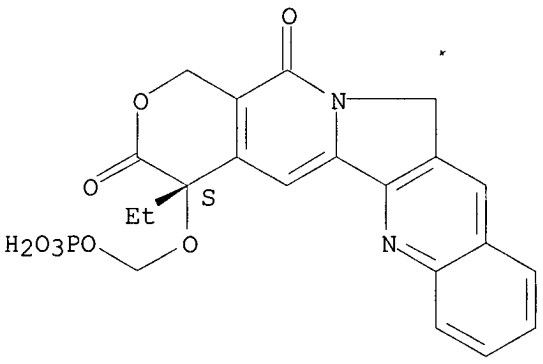


RN 258516-93-7 HCAPLUS
CN Methanol, [[3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl]oxy]-, dihydrogen phosphate, disodium salt (9CI) (CA
INDEX NAME)



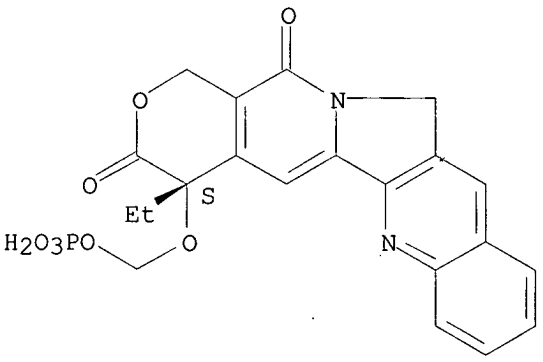
RN 258516-95-9 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-[(phosphonooxy)methoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 258516-97-1 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-[(phosphonooxy)methoxy]-, disodium salt, (4S)- (9CI) (CA INDEX NAME)

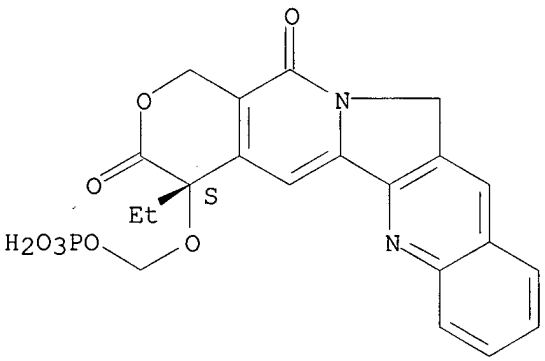
Absolute stereochemistry.



● 2 Na

RN 258516-99-3 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-[(phosphonooxy)methoxy]-, monosodium salt, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



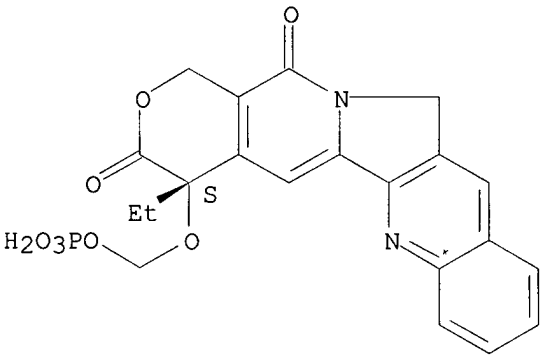
● Na

RN 258517-01-0 HCAPLUS
CN L-Lysine, compd. with (4S)-4-ethyl-4-[(phosphonooxy)methoxy]-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione (1:1) (9CI)
(CA INDEX NAME)

CM 1

CRN 258516-95-9
CMF C21 H19 N2 O8 P

Absolute stereochemistry.

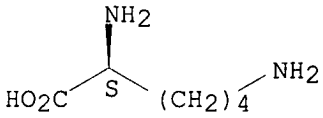


CM 2

CRN 56-87-1
CMF C6 H14 N2 O2
CDES 5:L

Absolute stereochemistry.

Searched by John Dantzman 703-308-4488

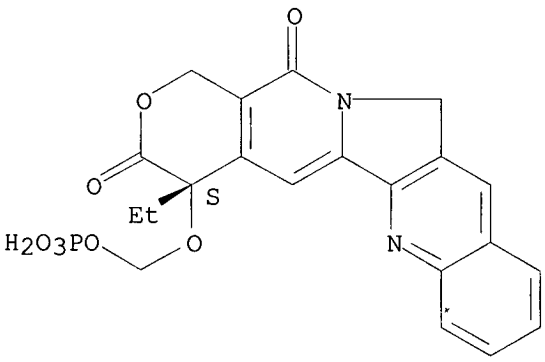


RN 258517-02-1 HCAPLUS
CN L-Arginine, compd. with (4S)-4-ethyl-4-[(phosphonooxy)methoxy]-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione (1:1) (9CI)
(CA INDEX NAME)

CM 1

CRN 258516-95-9
CMF C21 H19 N2 O8 P

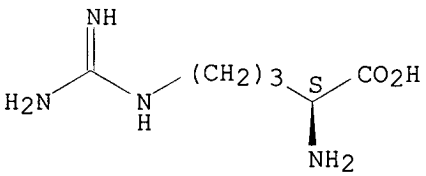
Absolute stereochemistry.



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2
CDES 5:L

Absolute stereochemistry.

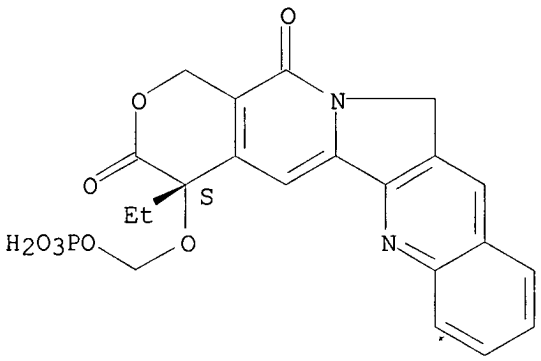


RN 258517-03-2 HCAPLUS
CN D-Glucitol, 1-deoxy-1-(methylamino)-, compd. with (4S)-4-ethyl-4-[(phosphonooxy)methoxy]-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 258516-95-9
CMF C21 H19 N2 O8 P

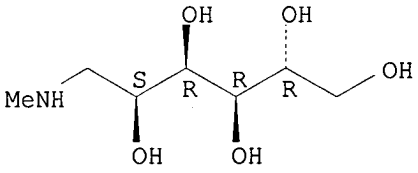
Absolute stereochemistry.



CM 2

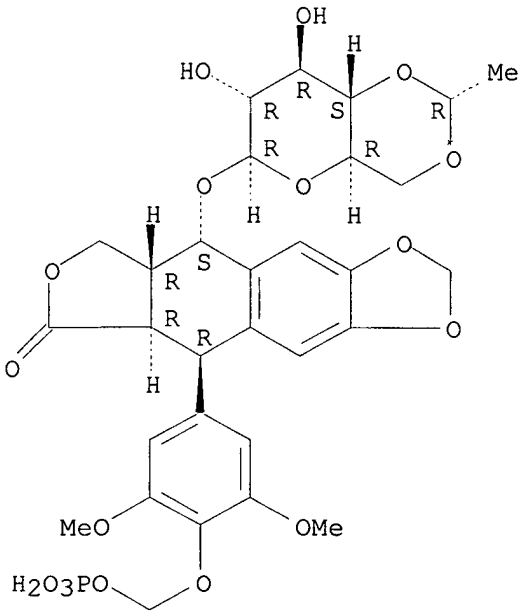
CRN 6284-40-8
CMF C7 H17 N O5
CDES *

Absolute stereochemistry.



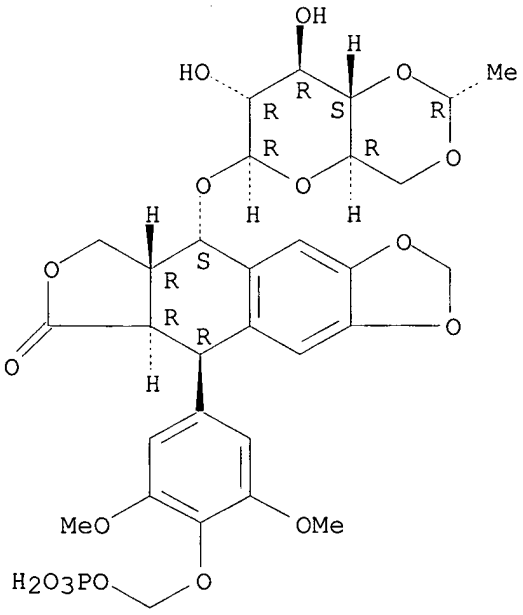
RN 258517-04-3 HCAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-[(phosphonooxy)methoxy]phenyl]-9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 258517-05-4 HCAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-[(phosphonooxy)methoxy]phenyl]-9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-, disodium salt, (5R,5aR,8aR,9S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

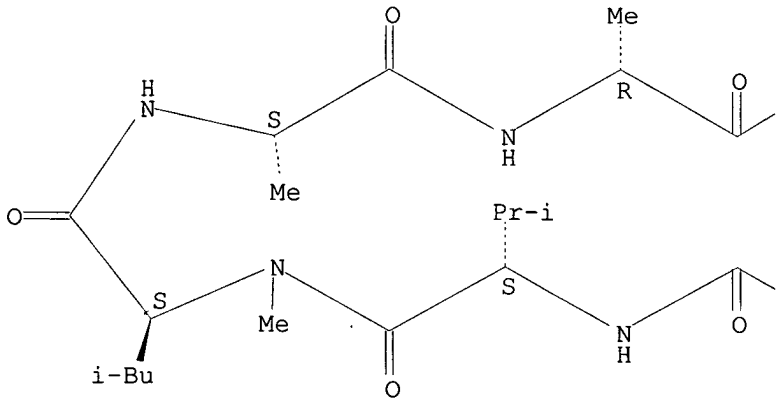


● 2 Na

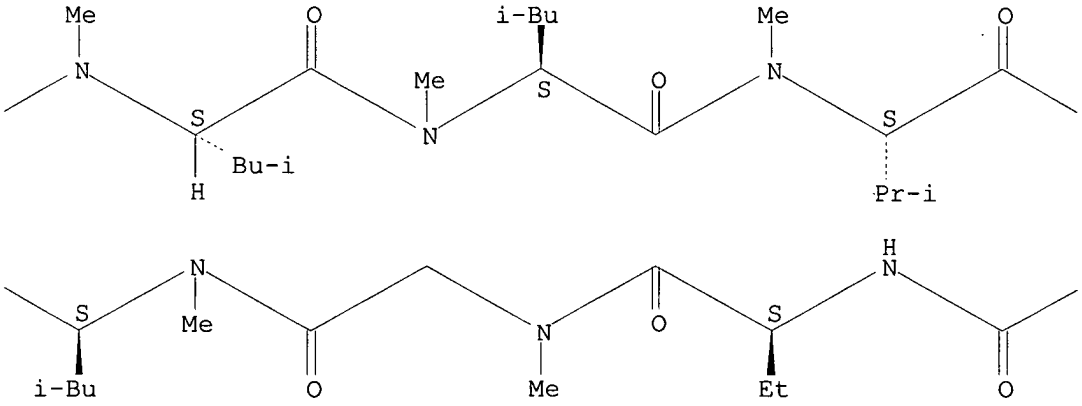
RN 258517-08-7 HCAPLUS
CN Cyclosporin A, 6-[(2S,3R,4R,6E)-4-methyl-2-(methylamino)-3-[(phosphonooxy)methoxy]-6-octenoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

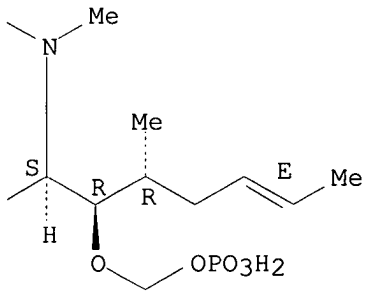
PAGE 1-A



PAGE 1-B

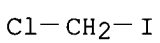


PAGE 1-C

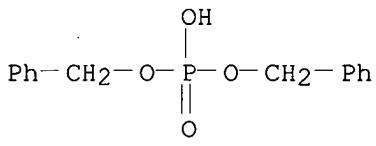


IT **9001-78-9**
RL: CAT (Catalyst use); USES (Uses)
(water-sol. prodrugs of hindered alcs. or phenols)
RN 9001-78-9 HCAPLUS
CN Phosphatase, alkaline (9CI) (CA INDEX NAME)

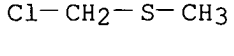
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **593-71-5**, Chloroiodomethane **1623-08-1**, Dibenzyl phosphate **2373-51-5**, Chloromethyl methyl sulfide **10191-41-0 16836-95-6**, Silver p-toluenesulfonate **50651-75-7**, Silver dibenzyl phosphate
RL: RCT (Reactant)
(water-sol. prodrugs of hindered alcs. or phenols)
RN 593-71-5 HCAPLUS
CN Methane, chloroiodo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 1623-08-1 HCAPLUS
CN Phosphoric acid, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

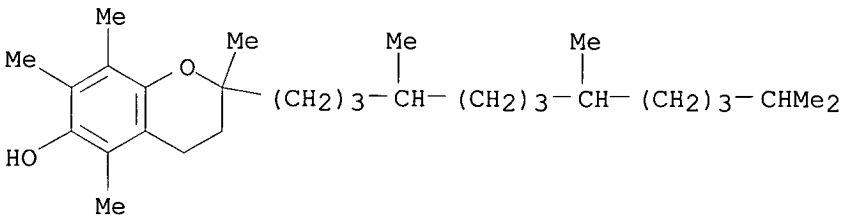


RN 2373-51-5 HCAPLUS
CN Methane, chloro(methylthio)- (9CI) (CA INDEX NAME)

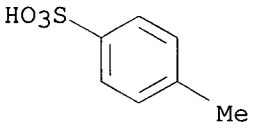


RN 10191-41-0 HCAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)- (9CI) (CA INDEX NAME)

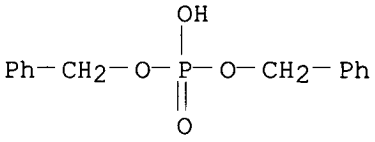


RN 16836-95-6 HCAPLUS
CN Benzenesulfonic acid, 4-methyl-, silver(1+) salt (9CI) (CA INDEX NAME)



● Ag(I)

RN 50651-75-7 HCAPLUS
CN Phosphoric acid, bis(phenylmethyl) ester, silver(1+) salt (9CI) (CA INDEX NAME)



● Ag(I)

IT **74418-05-6P 258516-17-5P 258516-21-1P**
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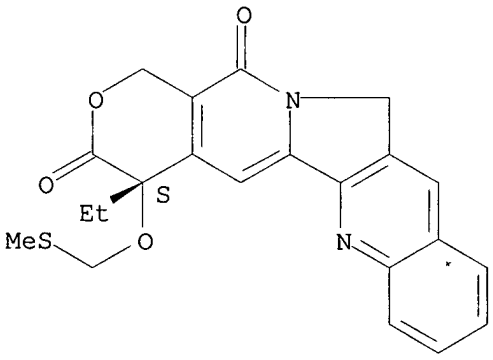
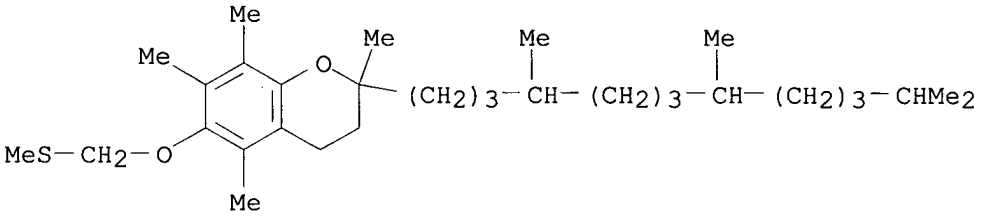
258516-51-7P 258516-55-1P 258516-58-4P
258516-61-9P 258516-64-2P 258516-67-5P
258516-69-7P 258516-72-2P 258516-75-5P
258516-78-8P 258516-80-2P 258516-82-4P
258516-84-6P 258516-85-7P 258517-06-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(water-sol. prodrugs of hindered alcs. or phenols)
RN 74418-05-6 HCAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-[(methylthio)methoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

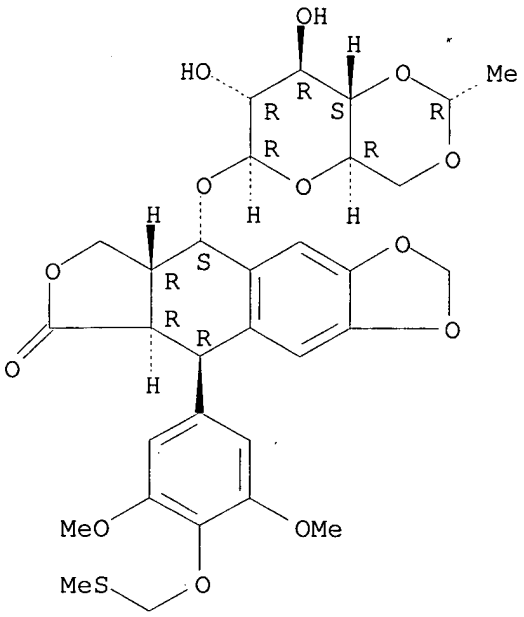


RN 258516-17-5 HCAPLUS
CN 2H-1-Benzopyran, 3,4-dihydro-2,5,7,8-tetramethyl-6-[(methylthio)methoxy]-2-(4,8,12-trimethyltridecyl)- (9CI) (CA INDEX NAME)



RN 258516-21-1 HCAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-[(methylthio)methoxy]phenyl]-9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

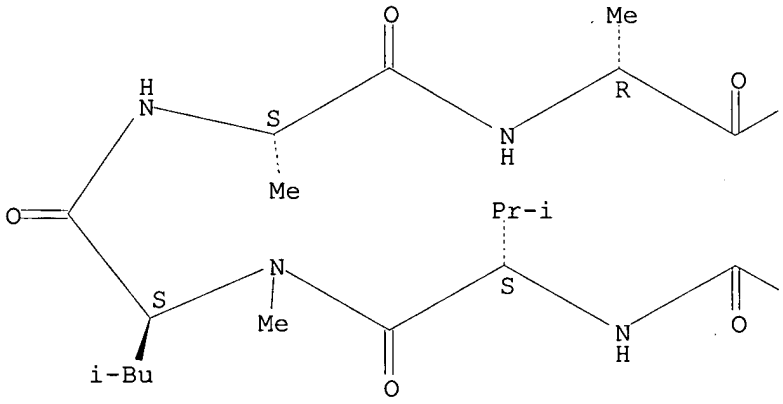
Absolute stereochemistry.



RN 258516-25-5 HCAPLUS
CN Cyclosporin A, 6-[(2S,3R,4R,6E)-4-methyl-2-(methylamino)-3-[(methylthio)methoxy]-6-octenoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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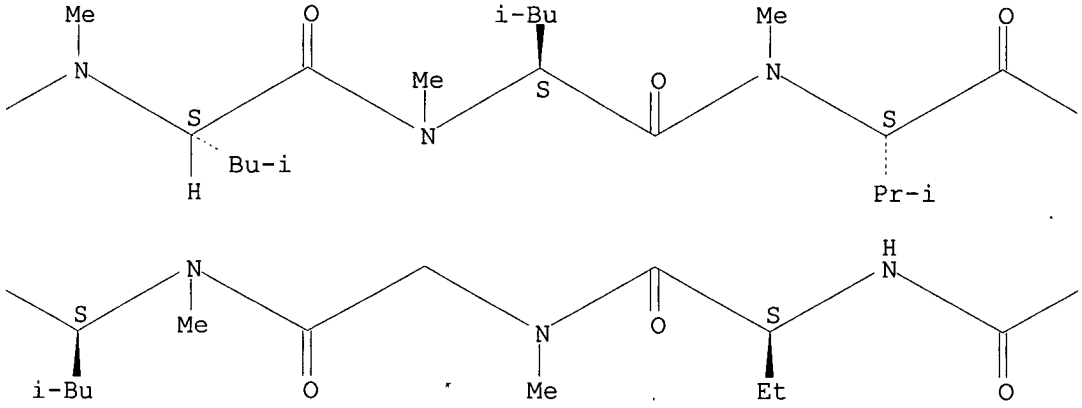
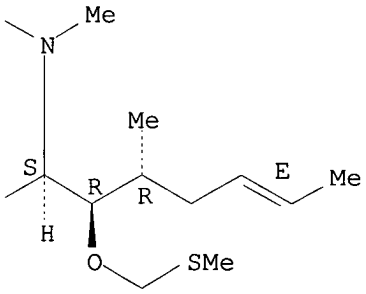
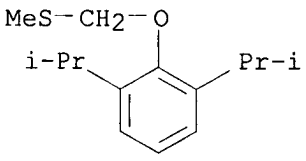


PAGE 1-C



RN 258516-32-4 HCAPLUS
CN Benzene, 1,3-bis(1-methylethyl)-2-[(methylthio)methoxy]- (9CI) (CA INDEX NAME)



RN 258516-36-8 HCAPLUS
CN Phosphoric acid, [[3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl]oxy]methyl bis(phenylmethyl) ester
(9CI) (CA INDEX NAME)

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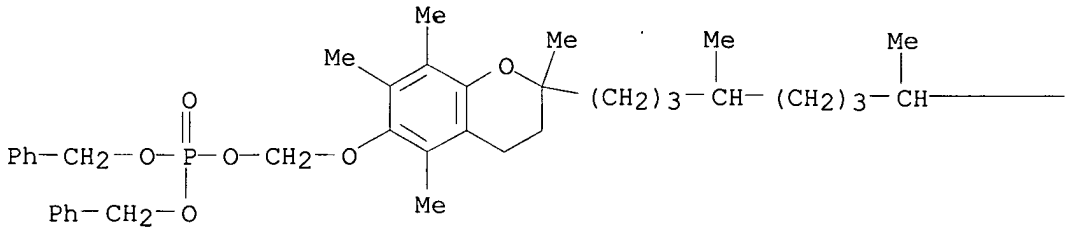

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— $(CH_2)_3$— $CHMe_2$

RN 258516-40-4 HCAPLUS
CN Phosphoric acid, 4-[(5R,5aR,8aR,9S)-9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,5a,6,8,8a,9-hexahydro-6-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]-2,6-dimethoxyphenyl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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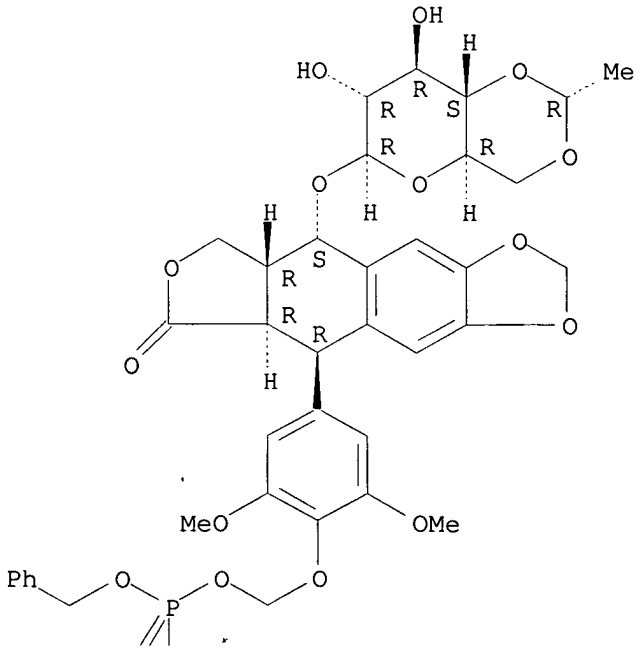

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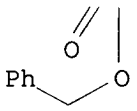

RN 258516-44-8 HCAPLUS
CN Cyclosporin A,
6-[(2S,3R,4R,6E)-3-[[[bis(phenylmethoxy)phosphinyl]oxy]meth
oxy]-4-methyl-2-(methylamino)-6-octenoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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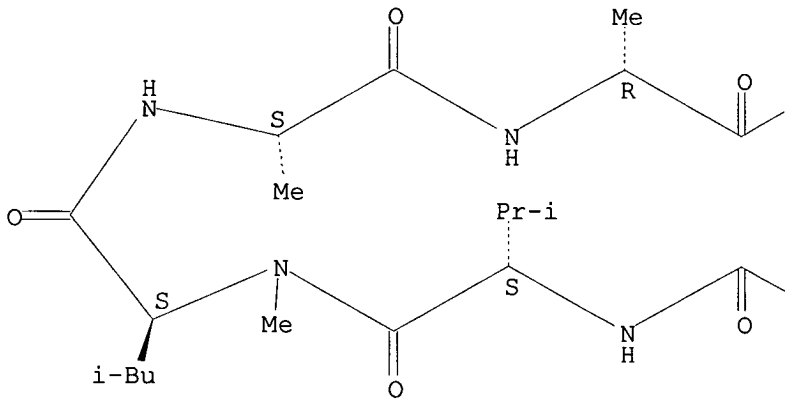

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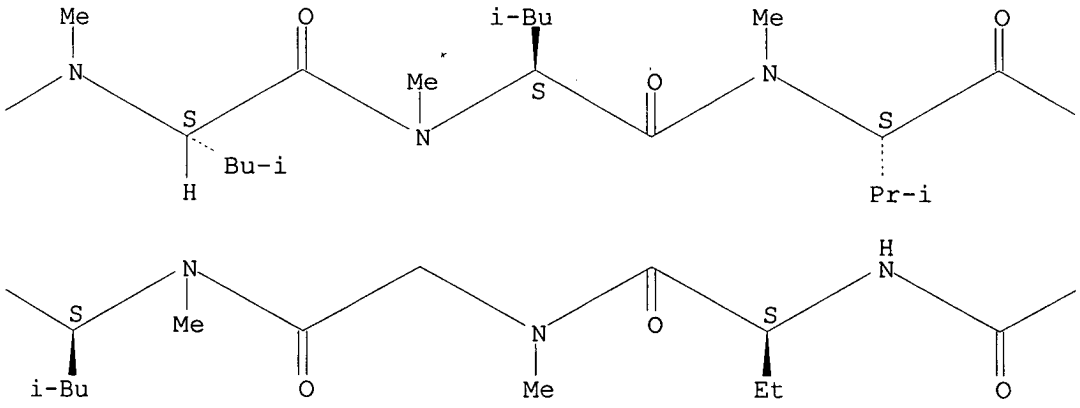

Searched by John Dantzman 703-308-4488

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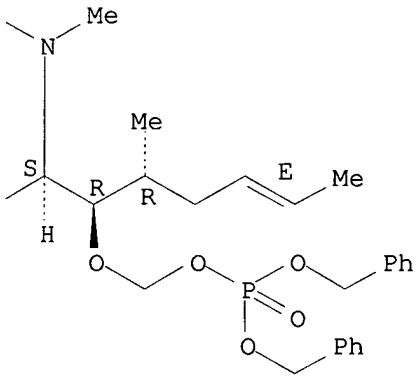
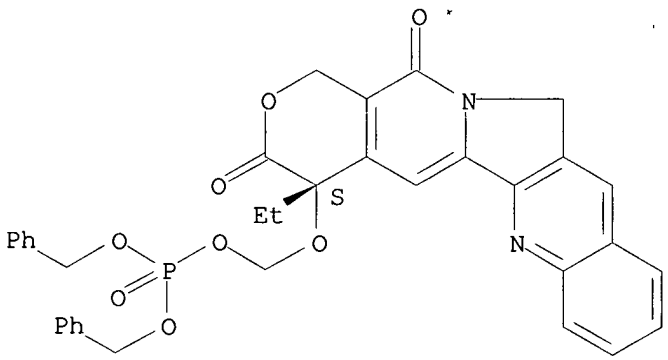
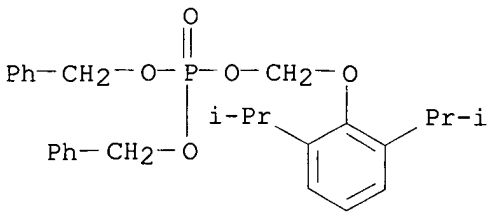


RN 258516-48-2 HCAPLUS
CN Phosphoric acid, [[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]methyl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 258516-51-7 HCAPLUS
CN Phosphoric acid, [2,6-bis(1-methylethyl)phenoxy]methyl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 258516-55-1 HCAPLUS
CN Phosphoric acid, [[3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl]oxy]methyl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

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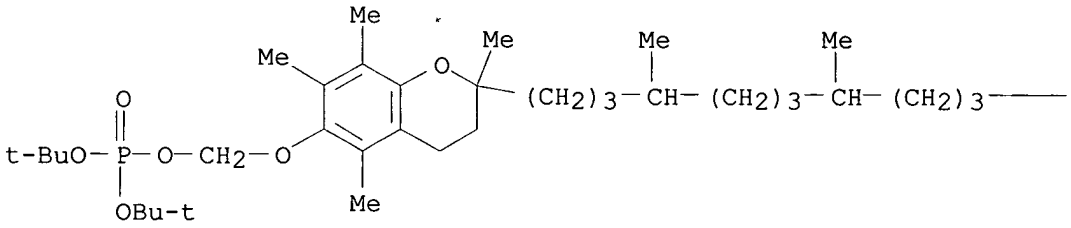

PAGE 1-B

— $CHMe_2$

RN 258516-58-4 HCAPLUS
CN Phosphoric acid, bis(1,1-dimethylethyl) 4-[(5R,5aR,8aR,9S)-9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,5a,6,8,8a,9-hexahydro-6-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]-2,6-dimethoxyphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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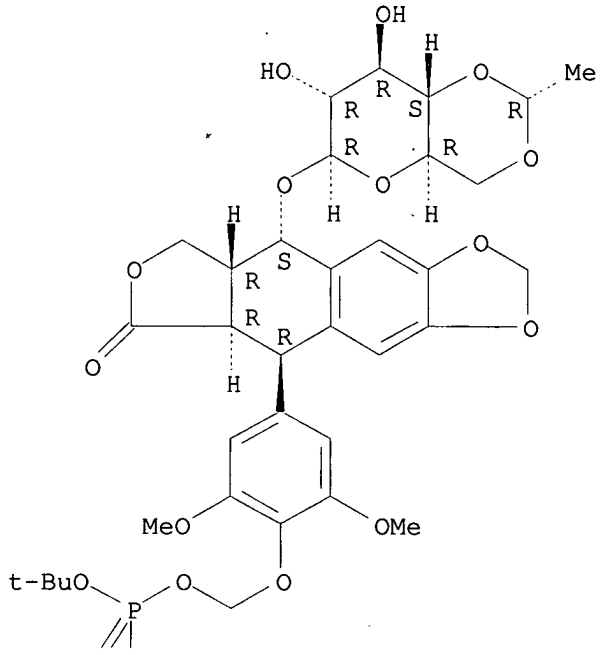

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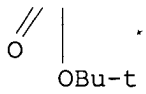

RN 258516-61-9 HCAPLUS
CN Cyclosporin A,
6-[(2S,3R,4R,6E)-3-[[[bis(1,1-dimethylethoxy)phosphinyl]oxy
]methoxy]-4-methyl-2-(methylamino)-6-octenoic acid]- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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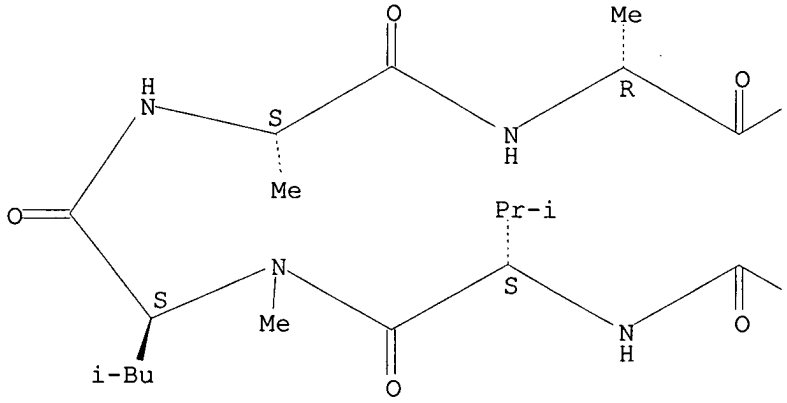

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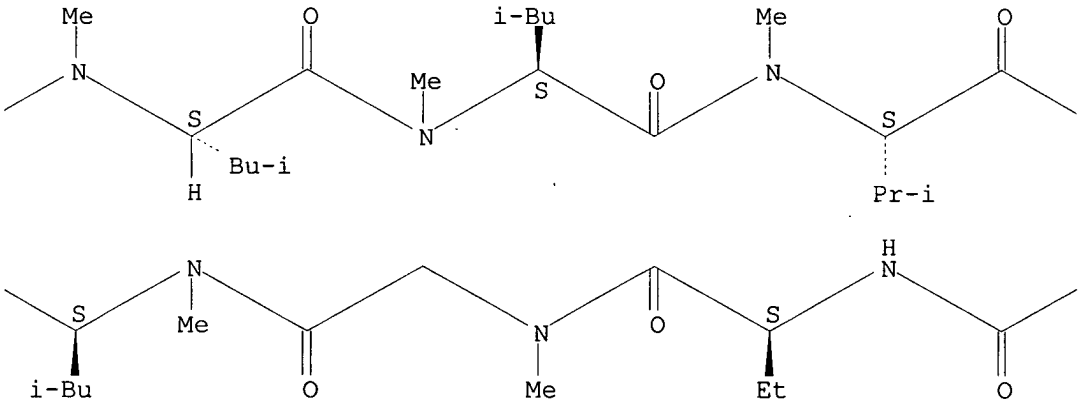

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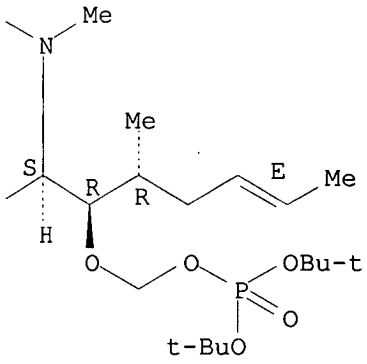
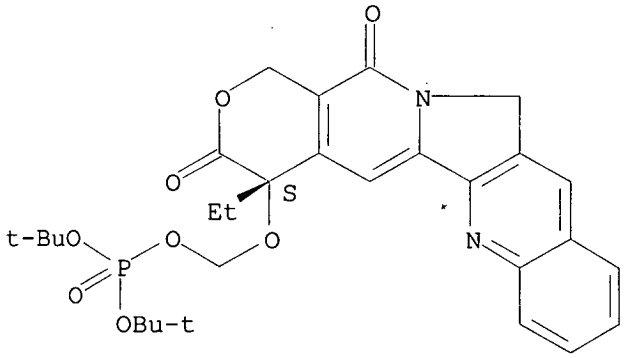
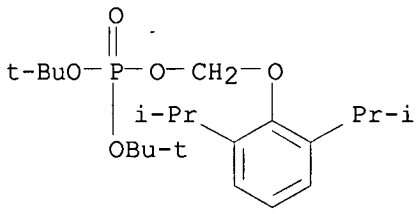


RN 258516-64-2 HCAPLUS
CN Phosphoric acid, bis(1,1-dimethylethyl) [[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 258516-67-5 HCAPLUS
CN Phosphoric acid, [2,6-bis(1-methylethyl)phenoxy]methyl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 258516-69-7 HCAPLUS
CN Phosphoric acid, [[3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-yl]oxy]methyl di-2-propenyl ester (9CI) (CA INDEX NAME)

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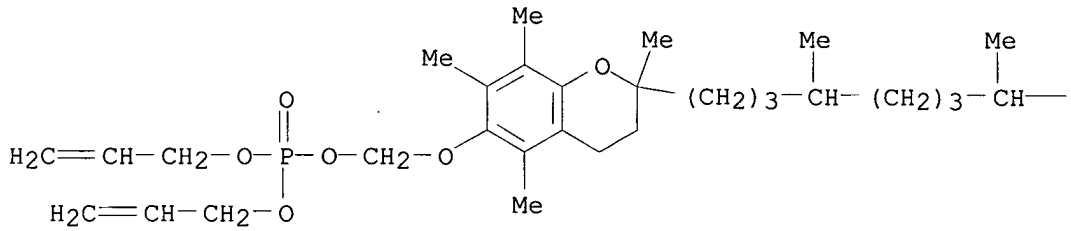

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— $(CH_2)_3$— $CHMe_2$

RN 258516-72-2 HCAPLUS
CN Phosphoric acid, 4-[(5R,5aR,8aR,9S)-9-[[4,6-O-(1R)-ethylidene-.beta.-D-glucopyranosyl]oxy]-5,5a,6,8,8a,9-hexahydro-6-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]-2,6-dimethoxyphenyl di-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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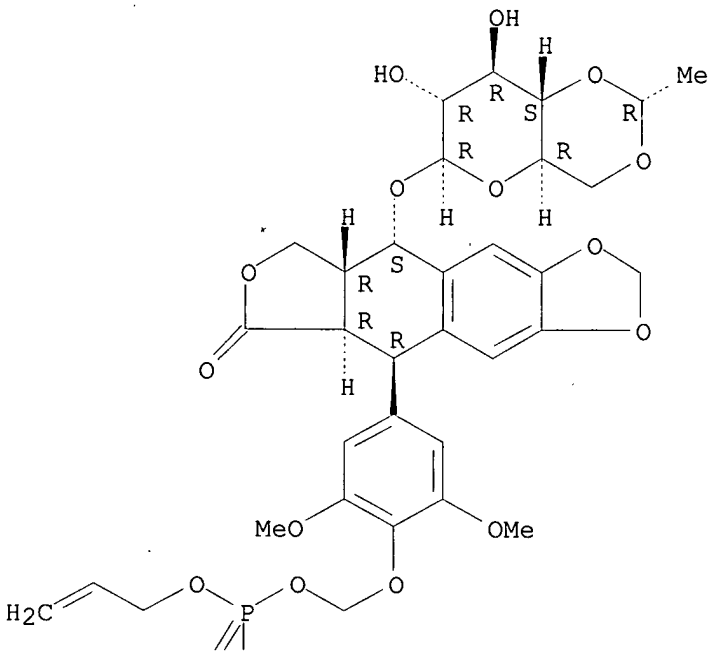

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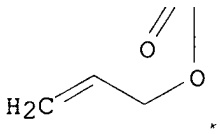
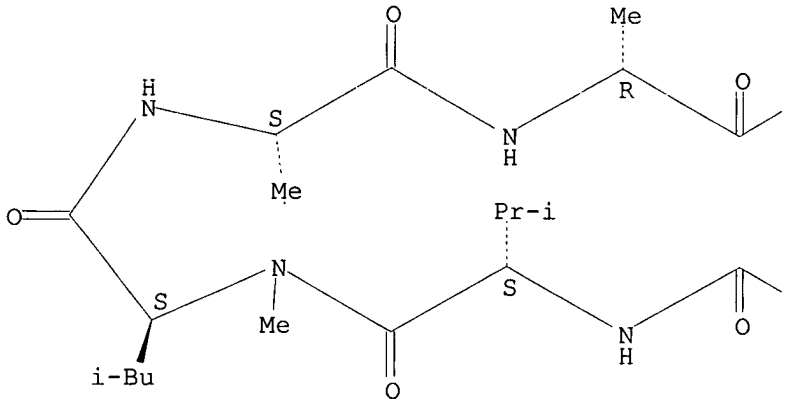


RN 258516-75-5 HCAPLUS
CN Cyclosporin A,
6-[(2S,3R,4R,6E)-3-[[[bis(2-propenyloxy)phosphinyl]oxy]meth
oxy]-4-methyl-2-(methylamino)-6-octenoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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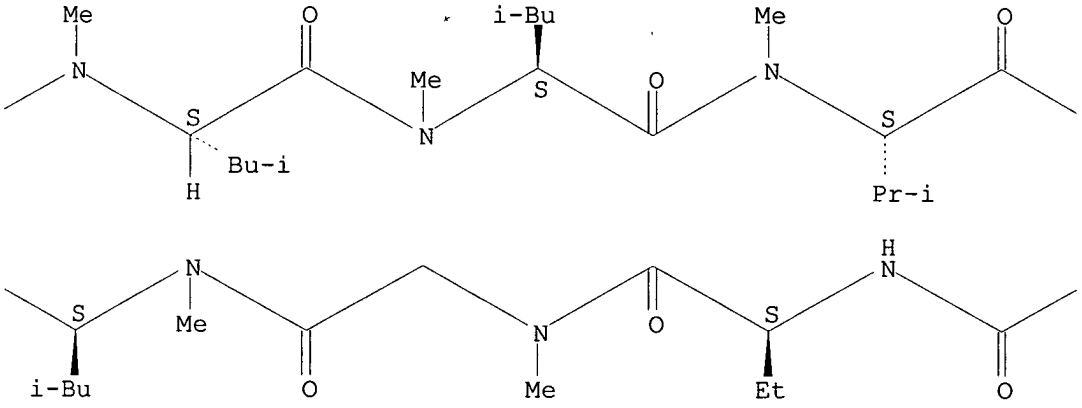

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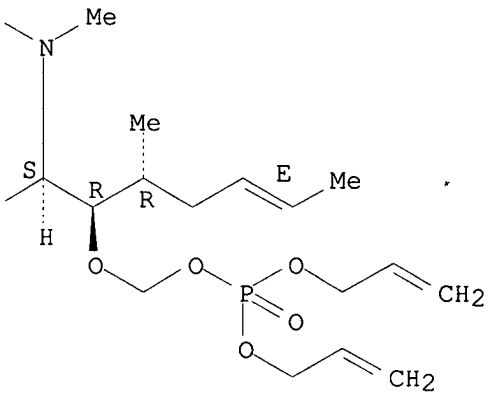
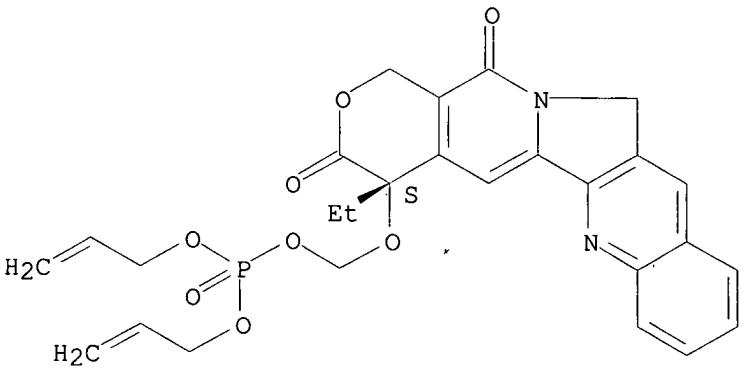
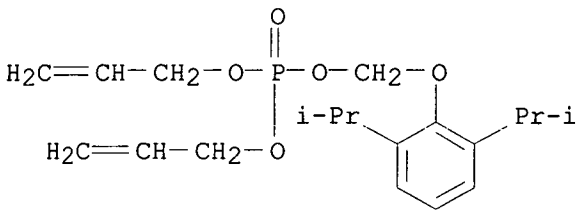


RN 258516-78-8 HCAPLUS
CN Phosphoric acid, [[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]methyl di-2-propenyl ester (9CI) (CA INDEX NAME)

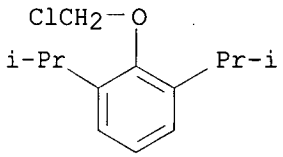
Absolute stereochemistry.



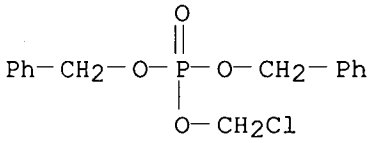
RN 258516-80-2 HCAPLUS
CN Phosphoric acid, [2,6-bis(1-methylethyl)phenoxy]methyl di-2-propenyl ester
(9CI) (CA INDEX NAME)



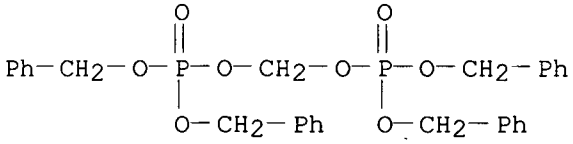
RN 258516-82-4 HCAPLUS
CN Benzene, 2-(chloromethoxy)-1,3-bis(1-methylethyl)- (9CI) (CA INDEX NAME)



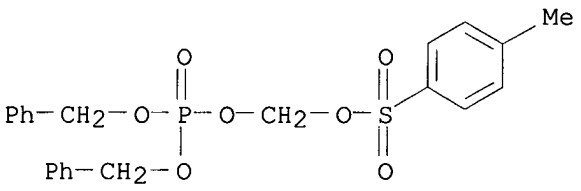
RN 258516-84-6 HCAPLUS
CN Phosphoric acid, chloromethyl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 258516-85-7 HCAPLUS
CN Phosphoric acid, methylene tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 258517-06-5 HCAPLUS
CN Phosphoric acid, [[(4-methylphenyl)sulfonyl]oxy]methyl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



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RE
(1) Bristol-Myers Squibb Co; EP 0604910 A 1994
(2) Bristol-Myers Squibb Co; EP 0639577 A 1995
(3) Bristol-Myers Squibb Co; EP 0747385 A 1996
(4) Golik, J; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1996, V6(15), P1837 HCAPLUS
(5) Safadi, M; PHARMACEUTICAL RESEARCH 1993, V10(9), P1350 HCAPLUS